UNIVERSITI TEKNOLOGI MARA

A STUDY ON ADVERSE DRUG REACTIONS RELATED TO DRUG-INDUCED LIVER TOXICITY IN MALAYSIA FROM 2012 TO 2014

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ABSTRACT

Background: Drug-induced liver toxicity studies in Malaysia are limited but now day toxicity involving liver caused by the drug is alarming. The number of cases reported of drug-induced hepatotoxicity is keep increasing and something should be done in order to control this ADR's from worsening.

Objectives: To study drugs that induced liver toxicity in Malaysia from the year 2012 to 2014. Besides that, the specific objectives is to determine the most common drug that induced liver toxicity during 2012 till 2014. In addition, this study aims to determine the severity and drug hepatotoxicity causal relationship as well as the predisposing factor of hepatotoxicity.

Methods: Data of ADR's involving hepatotoxicity was collected at Pharmacovigilance Section, Centre of Post Registration Product National Pharmaceutical Control Bureau (NPCB). There are 555 cases reported on drug-induced liver toxicity from the year 2012 to 2014 were extracted from MADRAC Quest 2 database. Based on WHO criteria, the causality and types of toxicity involved in liver injury were determined based on system organ classes: Liver and Biliary Disorder (code: 0700).

Results: Based on the results, the most drug that induced liver toxicity in those 3 years which is 2012 to 2014 are the anti-tubercular drug which shown that male is more likely to get hepatotoxicity with 310 cases; 55.9% reported from 555 cases and Malay is at highest risk with 41.3%. An elderly patient with age range 46 to 60 years old were the highest number of patient reported on drug inducing liver toxicity. Sabah was reported with the most cases reported on ADR's which 18% of 100 cases been reported while hepatic enzyme increased was the highest toxicity involving drug-induced liver toxicity with 178 cases; 32.1% reported. 2013 has the highest number of cases reported which is 242 cases. Extend of severity liver toxicity is moderate which 237 cases reported from 555 cases with probable causality with 44.5%. There were associations between age group, gender, and race with an extent of a severity of hepatotoxicity when the P value 0.0034, 0.000 and 0.000 respectively. The race was the only predictor for an anti-tubercular drug which induced liver toxicity when it showed Malay is at high risk to get adverse drug reaction related to drug caused hepatotoxicity.

Conclusion: Anti-tubercular drug such Isoniazid, Rifampicin, Pyrazinamide was the most common drug that induced liver toxicity in Malaysia based on cases of ADR'S reported from 2012 to 2014. To ensure adherence to therapy and monitoring hepatic dysfunction from occur, regular monitoring of therapy as well as liver chemistry in susceptible group of patient should be done in order to prevent drug induced hepatotoxicity in risky group since anti-TB drugs have the potential to cause hepatotoxicity.

CHAPTER ONE

INTRODUCTION

1.1 Overview

Liver is a main organ that has function to maintain the internal body environment (Pandit, Sachdeva, and Bafna, 2012). The liver is located behind the ribs in the upper right-hand parts of the abdomen, where it is in triangle shape which consists of two main lobes in dark reddish brown color. Usually in adult, the weight of the liver actually is about 3 pound and the size is like a football. In liver, there is a system called biliary system which consists of blood vessels and bile ducts that both of it is well organized which is connected with more than 300 billion of specialized cell. People who the liver is shutting down can only survive one or two days because if the liver fails to function it will affect the human body system. There is a special thing about the liver, which liver still can be functioning even if the liver is affected by the disease for about 75% or parts of the liver are being removed. This is the amazingly characteristic of the liver because the healthy part that remained in the body can regenerate new liver tissue (Singh, 2014).

The liver also plays a major role in maintaining the body performance and regulating the homeostasis of the human body. Besides that, the liver also involved in growth, fighting over disease, supplying the nutrient, providing energy and also part of the reproduction process. Metabolism of carbohydrate, fat and protein occur in the liver.